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NeuroScience and Service

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The brain has often been described, quite accurately, as one of the most complex objects in the natural world. Understanding its workings, to say nothing about intervening in them, is among the hardest problems in science. While this makes the challenge all the more enticing, in the short term, it acts to limit the impact that neuroscience can have on real-world problems. A comprehensive understanding of fundamental principles of brain function, and their translation into treatments for brain disorders, may be decades away. Even as we pursue these long-term goals, what are the prospects for our field to engage with some of the pressing challenges the world currently faces? An initiative that I have had the opportunity of being involved with, Project Prakash, illustrates one way forward. The operational model that it has adopted enables an immediate merging of basic research and societal service.

It is customary to classify research projects dichotomously as basic or applied. The former typically operate on longer timescales than the latter; basic projects seek to advance knowledge, while applied projects address specific real-world problems; one kind is about science, the other is about service. These differences are so pronounced that the two classes are generally considered irreconcilably distinct. This naturally leads to the conclusion that it is unrealistic, or even unfair, to expect basic research to engage with concrete problems with any immediacy. My position in this article is that contrary to this assumption, there exist opportunities for merging basic science and societal service. I illustrate my points using a project my laboratory has been engaged in over the past decade. The focus of my remarks on Project Prakash is not intended to aggrandize this specific initiative but simply to provide a concrete exemplar for ideas that may otherwise seem to be idealistic, but impractical, homilies. Project Prakash, I am convinced, is the tip of the proverbial iceberg of the many ways in which basic neuroscience can work simultaneously toward pushing the frontiers of knowledge as well as tackling, here and now, some of society's most pressing problems.

Project Prakash

The genesis of Project Prakash lies in the confluence of two pressing needs, one humanitarian and the other scientific.

The Humanitarian Need

According to the World Health Organization (WHO), nearly 90% of the world's blind live in the developing world. This population includes over one million children. Although a large proportion of the pediatric cases are treatable (due to conditions like congenital cataracts and corneal opacities), most children never receive medical care because of their poverty, the paucity of pediatric treatment facilities, and their remoteness from the villages where much of the population resides. The affected children face greatly elevated mortality rates (nearly 60% perish within a year of the onset of blindness; WHO, 2007) and severely diminished opportunities for education and eventual employment. For blind girls, the outlook is even direr. Many are confined at home, suffer abuse, and are denied contact with the outside world. There is, clearly, an urgent humanitarian need to identify and treat curably blind children and also to build awareness amidst the rural population regarding treatable and preventable blindness.

The Scientific Need

The provision of sight-restoring interventions to blind children only makes sense if the brain can in fact learn to make effective use of visual information despite several years of congenital blindness. What are the prospects of such learning? Our understanding of this issue has been based almost exclusively on studies conducted several decades ago to explore the effects of impoverished stimulation on non-human animals (e.g., Wiesel and Hubel, 1965; LeVay et al., 1980). The difficulties of comprehensively evaluating visual functions in animals limits the applicability of these studies for making predictions regarding prospects for recovery in human children. There is a need to directly assess how well the human brain can acquire visual function after many years of congenital blindness. This issue is of great significance for child health. As new eye treatments become available and existing treatments reach children and adults who are currently blind, the question of visual prognosis keeps gaining in importance. Addressing this issue also presents an unprecedented opportunity to explore some deep basic scientific questions: how does neural plasticity change as a function of age and how does the brain learn to extract meaning from sensory information.

The two needs are synergistic: the humanitarian mission benefits from the scientific quest and vice versa. Building on this synergy, Project Prakash's mission is to bring treatment to blind children and systematically examine the processes and prospects of their recovery.

Since the Project's founding in 2005, the Prakash team has operationalized this mission as a three-stage process: outreach, treatment, and study (Figure 1). The site of operations thus far has been India, which is home to one of the largest populations of blind children in the world. Outreach involves organizing regular pediatric ophthalmic screening camps in

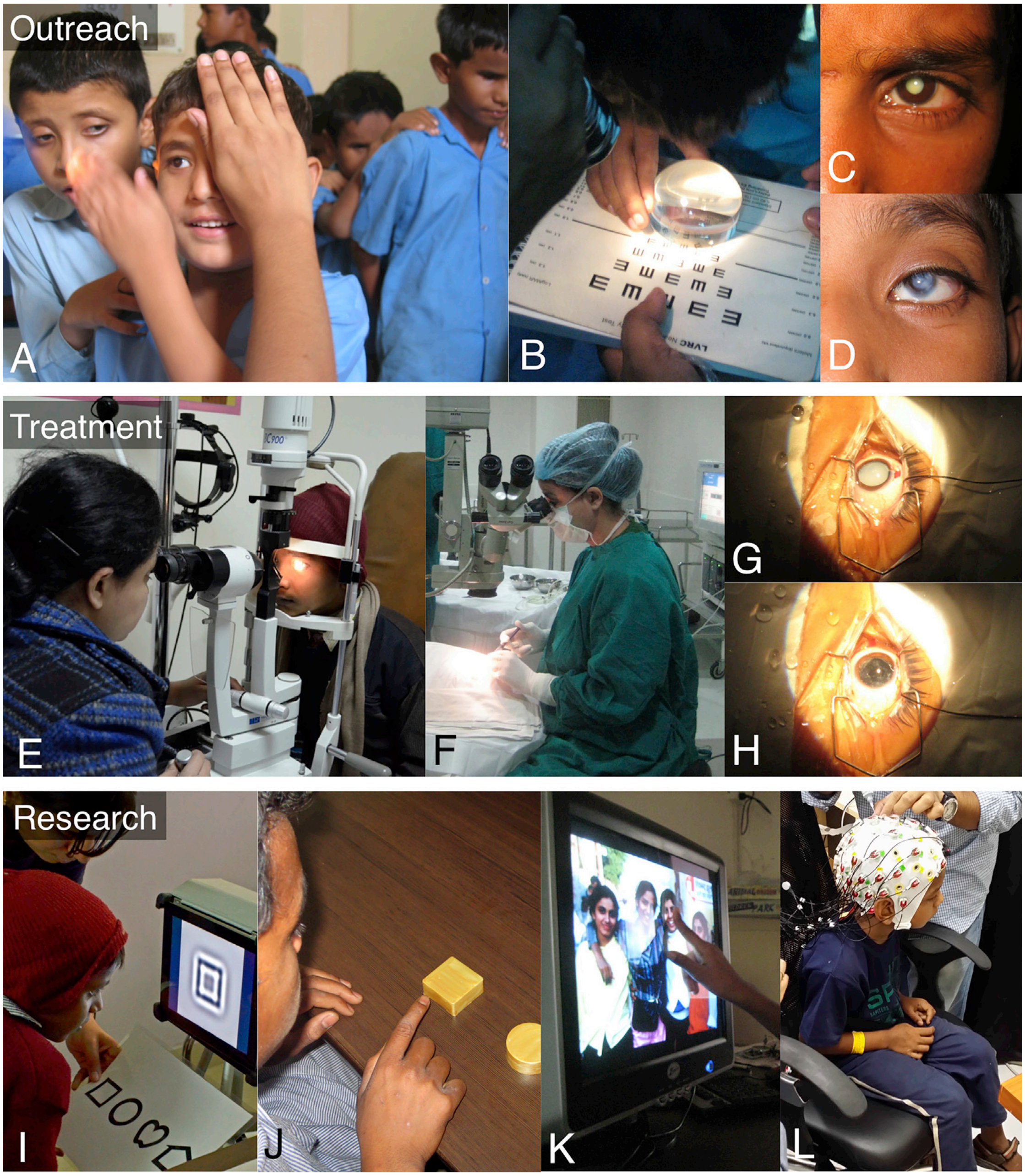

Figure 1. The Three Components of Project Prakash: Outreach, Treatment, and Research
(A) Children at a screening camp conducted in a school for the blind.
(B) During the screening camps, we often come across children who are not completely blind but have "low vision" Such children are provided low-vision aids, such as magnifiers.
(C and D) The screening camps allow us to find children who suffer from treatable forms of blindness, such as cataracts (C) and corneal opacities (D).
(E) With a thorough ophthalmic examination at the hospital, we assess the child's fitness for surgery.
(F) Surgery involves cataract excision and insertion of a synthetic intra-ocular lens or corneal grafting.
(G and H) An eye before (G) and after (H) removal of cataract.
(I) Basic post-operative vision testing to assess acuity and contrast sensitivity.
(J) A child participates in a study investigating Molyneux's query.
(K) Assessment of face localization in scenes.
(L) A child participating in an electroencephalogram (EEG) study to investigate the development of visual responses to different categories of stimuli.

rural areas. A team of community liaisons, primary healthcare workers, optometrists, and ophthalmologists conducts each camp. Children are screened for a range of conditions, including severe refractive errors, ocular infections, and blindness. Candidates for treatment are brought to the Shroff Charity Eye Hospital (SCEH) in New Delhi for a more thorough secondary examination. A date for surgery is set in consultation with the child's guardian. Surgical treatment under stringent quality controls is provided in SCEH's world-class facilities. All expenses are borne by Project Prakash, which in turn is funded by the National Eye Institute (NIH), the Nick Simons Foundation, and several individual donors.

Treatment is followed by longitudinal studies of visual function. It is important to point out that the provision of treatment is never contingent on an agreement to participate in subsequent research studies. The studies involve standard assessments of basic visual function, specially designed tests of high-level vision and non-invasive brain imaging using fMRI. In this way, Project Prakash seeks to fulfill its mission of bringing light into the lives of curably blind children and, simultaneously, illuminating several key scientific questions about how the brain develops and learns to see. Hence, the name "Prakash," which in Sanskrit means light. The composition of the Prakash team reflects the Project's dual mission: a combination of researchers at the cutting edge of vision science, highly qualified ophthalmologists, healthcare workers with extensive field knowledge, and experts in non-invasive imaging technology.

Project Prakash has had tangible impacts on children's lives as well as on basic science. On the scientific front, one of the most compelling and far-reaching results from Project Prakash is evidence of recovery even after prolonged congenital blindness. These data provide valuable clues regarding brain plasticity and time lines of learning. Previous studies have demonstrated dramatic consequences of abnormal early visual experience on cortical function and visual behavior in mammals. Analogous data from humans have been much harder to come by. They have included rare case studies (Gregory and Wallace, 1963; Kurson, 2008) and results from children who suffered brief periods of blindness as infants (Lewis and Maurer, 2009). Project Prakash has provided an opportunity to build on and extend these important studies by systematically examining the functional consequences of prolonged visual deprivation on the human brain. Having followed the post-operative development of several children, Prakash researchers have found that while some aspects of vision, such as acuity and contrast sensitivity, are compromised by a history of deprivation (Ganesh et al., 2014; Kalia et al., 2014), there is pervasive evidence of skill acquisition on a variety of functional vision tasks ranging from simple shape matching to object and face recognition (Ostrovsky et al., 2006, 2009; Bouvrie and Sinha, 2007; Gandhi et al., 2014, 2015). The human brain, these findings suggest, retains an impressive ability to launch programs of visual learning well after the normal period of their deployment has passed. Complementing our behavioral studies, we have recently begun employing non-invasive brain imaging technology, specifically fMRI, to examine the kinds of cortical changes that accompany the very initial stages of human visual learning. This issue is operationally difficult to address in the conventional setting given the severe challenges of conducting brain imaging studies with newborn infants. Our neuroimaging studies so far have revealed that the onset of patterned visual information results in rapid modification of the ventral visual stream, even in individuals who have been congenitally blind for the first two decades of their lives. These results have significance for basic neuroscience as well as the practice of pediatric ophthalmology and the implementation of late stage blindness treatment programs.

From demonstrating the existence of recovery, the Prakash team has moved on to understanding the process of recovery. Their longitudinal studies with the Prakash children reveal that recovery unfolds in a systematic sequence. The age of treatment appears to modulate the duration of this process, but not its basic plan. The elucidation of this arc of development opens up the possibility of mechanistically specifying how visual bootstrapping happens; how do complex visual skills derive from simpler ones that precede them in developmental chronology. Along these lines, our results have highlighted the profound significance of dynamic information processing as a building block for other visual skills (Ostrovsky et al., 2009). This work simultaneously helps us understand how the human brain comes to meaningfully parse natural imagery while also providing guidelines for the development of computational models of complex visual learning (Sinha et al., 2009).

Given the unusual visual trajectory of these children, Project Prakash has had the opportunity to empirically address some questions that until now were largely thought experiments. The famous "Molyneux Query" is a case in point. For the brain, the onset of sight sets up the challenge of correlating visual information with those from other sensory modalities, such as touch and audition. Is this linkage established via innate "amodal" processes or via a process of learning? This foundational question, which was framed over three centuries ago by philosophers such as John Locke and William Molyneux (Locke, 1690), is central to understanding the nature of internal representations and the nativism versus empiricism debate. The question has remained tantalizingly open ever since its formulation. With Project Prakash, we have precisely the kinds of individuals who could help address this issue directly. The answer has turned out to be remarkably interesting. After showing no evidence of cross-modal transfer immediately after the onset of sight, the Prakash children achieve proficiency in periods as short as a week (Held et al., 2011). This points to the existence of rapid learning processes for detecting relationships across sensory streams (Sinha et al., 2014a). This has been a particularly gratifying result, not only because of the historical heft and theoretical significance of the question, but also because it emerged from an undertaking that brought the gift of sight to blind children.

Project Prakash has yielded scientific dividends that go beyond the domain of visual development. One of the most gratifying, and unexpected, of these is a conjecture regarding autism. Some similarities in the sensory processing styles

Figure 2. Project Prakash's Impact on Children's Lives
(A and B) A young girl before (A) and after (B) sight surgery.
(C) Independence and mobility. Four Prakash participants, who were treated a few years ago, head to the railway station for a 400-mile-long journey home. They had come to the hospital in Delhi to meet the Prakash team for periodic progress monitoring.
(D) Creative expressions. Paintings done by Prakash children exhibited in the Butler Gallery at Princeton University.

of the newly sighted children on the one hand and autistic children on the other led us eventually to the hypothesis of a predictive impairment in autism (Sinha et al., 2014b). This idea has helped guide the design of targeted empirical studies of autism and, more broadly, has the potential to help improve our understanding of the condition by providing a unifying account of several aspects of its complex phenotype.

Overall, we are excited about the information about developmental dynamics our behavioral and neuro-imaging studies are providing. The results paint a picture of a brain that remains impressively adaptable well into life and that can reorganize itself quite rapidly to allow a newly sighted child to make use of the novel sensory information received from the eyes. These early results provide the foundation for a rich set of studies that are sure to help us better understand the processes by which we acquire our impressive visual abilities.

Societal Impact

Besides providing novel insights regarding basic questions in experimental and theoretical neuroscience, Project Prakash has also yielded more pragmatic benefits.

Project Prakash has directly contributed to improving children's health (Figure 2). The Project's outreach effort has, to date, provided ophthalmic screening to over 40,000 children residing in some of north India's poorest and most neglected villages. Over 450 of these children have been provided surgical treatment for congenital blindness and nearly 1,500 have received non-surgical care for conditions like eye infections and severe refractive errors. Over the past year, we conducted Quality of Life surveys with 77 Prakash children to examine how different facets of their lives are affected by the onset of sight. The results were very encouraging. On all dimensions of assessment (independence, mobility, and societal attitudes), a significant majority of the children reported improvements after gaining sight.

The outreach efforts of our project have allowed us to bring the benefits of modern medicine to several of the most medically neglected and financially impoverished rural communities. Each screening camp has also served an educational purpose by informing villagers of various ocular diseases and options for their prevention as well as treatment. This has served to counteract superstitions and reliance on unqualified quacks, as well as de-stigmatize blindness. Such increased awareness is likely to help decrease the incidence of treatable/preventable blindness in the years to come.

The Prakash finding that several children languishing in schools for the blind can in fact gain vision has initiated policy changes regarding the criteria for admission to such schools. As a consequence of Project Prakash, a writ petition was filed in the Supreme Court of India to mandate thorough ophthalmic examinations of all children prior to their enrollment in a school for the blind. Project Prakash has also helped focus attention in governmental circles on pediatric blindness. The Ministry of Health asked for a report on incidence and treatment of childhood blindness in each Indian state after a question was raised in the parliament as a direct consequence of results from Project Prakash reported in a prominent newspaper. In the clinic, Prakash findings demonstrating significant visual recovery even after extended congenital blindness are precisely the principled inducements ophthalmologists need to provide treatment to older children, whom they might otherwise have considered to be past the "critical age."

The response of the neuroscience community, and of society more broadly, to this initiative has been enthusiastic, as indicated by the fact that Project Prakash has been featured as a Presidential Lecture during a Society for Neuroscience meeting and also highlighted in several prominent journals (Lok, 2014; Chatterjee, 2015). The Project seems to especially strike a chord with the young trainees who are embarking on their exploration of neuroscience. Invariably, they come into the field with idealistic notions of impacting science and society. Here is an e-mail that I recently received from a doctoral student in Germany:

> I am nearly on the verge of quitting. I really want to contribute and make a difference, even if it is really small. However, I need to "see" the difference I make. This email is not really to ask for a job but perhaps to get ideas from you, about how to put my knowledge of biology and desire for social work to good use. This is an effort from my side to motivate myself as well, to finish my Ph.D. and finally attempt to make an actual difference.

The idealism that drives this note is plainly evident. Also evident is its risk of being extinguished. To the extent that Project Prakash can reassure young scientists that a merging of science and service is indeed possible, it serves as an important proof of principle of the ideal that draws many to science. And, in doing so, it makes it more likely that the young scientists themselves will explore avenues that can have a positive impact on the world they inhabit. This "lighting of many lamps" may well be one of Project Prakash's most significant legacies.

Other "Prakash" Opportunities

Project Prakash, with its focus on bringing sight to blind children, is just one instance of the many opportunities for neuroscience to merge science and service. Two other significant possibilities involve education and nutrition.

Despite ongoing efforts on the part of private and governmental organizations, illiteracy is distressingly rampant. According to UNESCO, nearly 900 million people across the world are incapable of reading or writing (women account for 63% of this number). Illiteracy leads to a cascade of effects, severely compromising prospects for individuals, their families, and even the nations they inhabit. The humanitarian need is clear: to provide education to illiterate individuals. In fulfilling this need, neuroscience has the opportunity to address several interesting questions. How would the brain respond to and represent structured knowledge late in life? How do these late acquired representations differ from those instantiated early in life? What aspects of cognition are most affected by the onset of literacy? How do the rates of learning disabilities compare for early and late literate populations? Progress on these questions will proceed hand in hand with the provision of literacy to those who have been denied it thus far.

Another "Prakash opportunity" concerns nutrition. It strains credulity to note that nearly half of all deaths of children under five years of age are due to malnourishment. In other words, three million children die each year due to an abject lack of food (according to UNICEF). The nutritional deprivation starts early, with maternal malnourishment leading to low birth weight of infants, and greatly enhancing their risk for infections, learning disabilities, mental retardation, and blindness. The obvious intervention is to eliminate food scarcity. While this is a big goal that seems perennially out of reach despite the many well-meaning efforts, we, as neuroscientists, can take charge of some important sub-components. We can examine, for instance, how various nutrients delivered to expectant mothers, as well as children across a spectrum of ages, impact different neural subsystems and associated cognitive functions. Which nutrients are most effective at different time points? Not only would the results be insightful about neural plasticity and agents promoting neural health, they would also provide objective criteria that can be used to evaluate different nutritional interventions.

The Road Ahead

When tackling a significant societal problem, a Prakash-like effort should have the ambition and courage to scale beyond the magnitude of a typical lab-based research project. All of us on the Prakash team are struck by how little it takes to fundamentally transform a child's life. Knowing this, and also knowing the vast numbers of children who currently languish without treatment, we feel that it is a moral imperative for us to enhance our efforts. The road ahead has to be traversed with even more vigor than the journey so far. How might we do so?

We believe that the way forward is to create a Prakash network. Several medical and research institutions, in India and other countries, have expressed an interest in partnering with Project Prakash. Having a network of such facilities within and beyond India with substantial outreach efforts in each and a well-coordinated exchange of clinical, scientific, and logistical information across them can be a true game changer. The robust science that can emerge from large multi-center studies, the refinement of clinical practices, and the enhanced efficiency of outreach efforts make this idea very appealing. Add to this the message that this would send out to the world at large of neuroscientists, clinicians, educationists, and students coming together across national boundaries to tackle one of humanity's biggest challenges, and the idea progresses from one that is simply appealing to one that must be realized.

We call this "Global Prakash" with the ambitious goal of eradicating treatable childhood blindness across the world. This would be one of the largest collective efforts to comprehensively tackle a pressing global healthcare issue. It would bring millions of children within the fold of modern medical care and lay the groundwork for other such large-scale efforts. In a very real sense, Global Prakash would bring light that transforms our lives as individuals and as nations. The rich corpus of data that will emerge from Global Prakash would not only be invaluable from the perspective of neuroscience, but it will also provide a foundation for launching new efforts in fields as diverse as epidemiology, health policy, child and maternal health, and anthropology.

And, turning inward, Global Prakash will likely be transformative for all of us who are fortunate enough to be involved. Realizing that the child you are seeing running and playing is the same one who had to be led by the hand just a few months ago, and that you had some role to play in this transformation, is an experience that profoundly changes how one thinks about the world and one's place in it.

Like childhood blindness, there are several daunting challenges that need addressing urgently. For at least some of them, we, as neuroscientists, can be instrumental in bringing together the resources, expertise, and commitment needed to mount appropriate responses. In doing so, we shall have an opportunity to fulfill the twin goals that motivate and animate us all: to be good scientists as well as good Samaritans.

ABOUT THE AUTHOR

Pawan Sinha is a professor of vision and computational neuroscience in the Department of Brain and Cognitive Sciences at MIT. Using a combination of experimental and computational modeling techniques, research in Professor Sinha's laboratory focuses on understanding how the human brain learns to recognize objects through visual experience.

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REFERENCES

Bouvrie, J.V., and Sinha, P. (2007). Neurocomputing *70*, 2218–2233.

Chatterjee, R. (2015). Science *350*, 372–375.

Gandhi, T.K., Ganesh, S., and Sinha, P. (2014). Psychol. Sci. *25*, 693–701.

Gandhi, T., Kalia, A., Ganesh, S., and Sinha, P. (2015). Curr. Biol. *25*, R358–R359.

Ganesh, S., Arora, P., Sethi, S., Gandhi, T.K., Kalia, A., Chatterjee, G., and Sinha, P. (2014). Br. J. Ophthalmol. *98*, 1424–1428.

Gregory, R.L., and Wallace, J.G. (1963). Recovery from Early Blindness: A Case Study (Heffers).

Held, R., Ostrovsky, Y., de Gelder, B., Gandhi, T., Ganesh, S., Mathur, U., and Sinha, P. (2011). Nat. Neurosci. *14*, 551–553.

Kalia, A., Lesmes, L.A., Dorr, M., Gandhi, T., Chatterjee, G., Ganesh, S., Bex, P.J., and Sinha, P. (2014). Proc. Natl. Acad. Sci. USA *111*, 2035–2039.

Kurson, R. (2008). Crashing Through: The Extraordinary True Story of the Man Who Dared to See (Random House).

LeVay, S., Wiesel, T.N., and Hubel, D.H. (1980). J. Comp. Neurol. *191*, 1–51.

Lewis, T.L., and Maurer, D. (2009). Optom. Vis. Sci. *86*, 640–646.

Locke, J. (1690). An Essay Concerning Human Understanding, First Edition (Thomas Bassett).

Lok, C. (2014). Nature *513*, 160–162.

Ostrovsky, Y., Andalman, A., and Sinha, P. (2006). Psychol. Sci. *17*, 1009–1014.

Ostrovsky, Y., Meyers, E., Ganesh, S., Mathur, U., and Sinha, P. (2009). Psychol. Sci. *20*, 1484–1491.

Sinha, P., Balas, B.J., and Ostrovsky, Y. (2009). Visual object discovery. In Object Categorization: Computer and Human Vision Perspectives, S. Dickinson and M. Tarr, eds. (Cambridge University Press).

Sinha, P., Wulff, J., and Held, R. (2014a). Establishing cross-modal mappings: empirical and computational investigations. In Sensory Integration and the Unity of Consciousness, D. Bennett and C. Hill, eds. (MIT Press).

Sinha, P., Kjelgaard, M.M., Gandhi, T.K., Tsourides, K., Cardinaux, A.L., Pantazis, D., Diamond, S.P., and Held, R.M. (2014b). Proc. Natl. Acad. Sci. USA *111*, 15220–15225.

Wiesel, T.N., and Hubel, D.H. (1965). J. Neurophysiol. *28*, 1029–1040.

World Health Organization (2007). Vision2020: The Right to Sight Action Plan (WHO Press).